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BOOK OF ABSTRACTS

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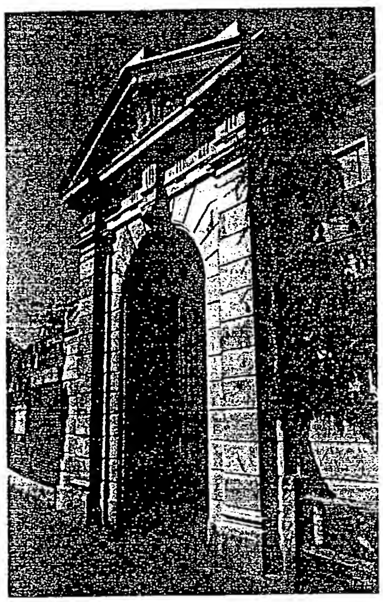

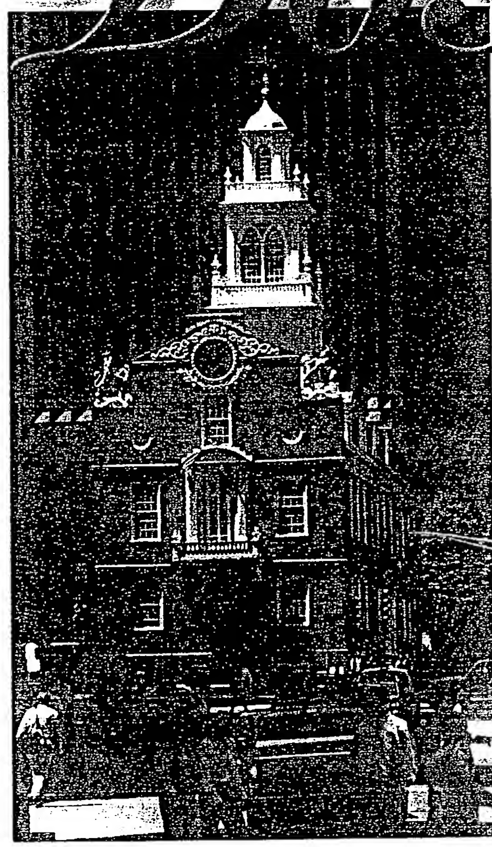

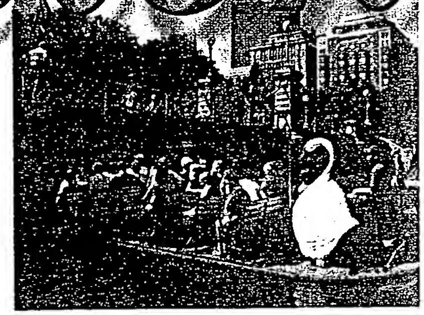

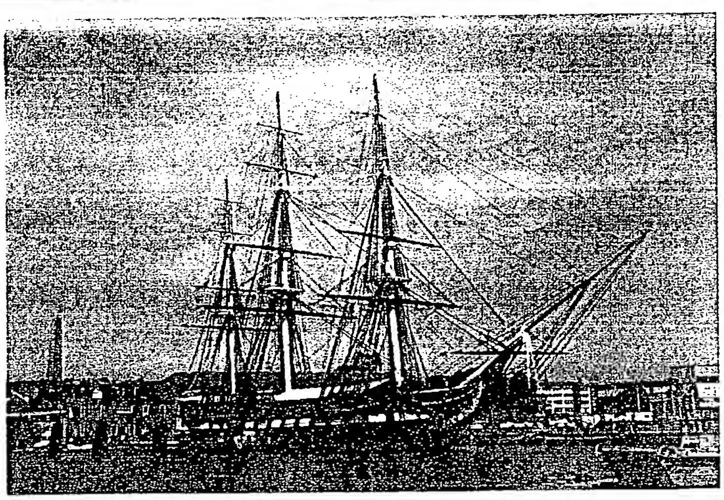

American Chemical Society

224TH ACS NATIONAL MEETING

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ABSTRACTS OF PAPERS

Part 1

224th ACS National Meeting

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American Chemical Society

Boston, MA

August 18-22, 2002

54.

PEPTIDES AS FLAVORANTS. ***Wilhelm Pickenhagen**, Corporate Research Division, DRAGOCO Gerberding & Co. AG, 37601 Holzminden, Germany, Fax: +49-5531-971158, doris.gattermann@eu.dragoco.com*

The sensory impression of flavor is stimulated by interaction of volatile and non-volatile materials with the chemoreceptors taste and smell. Whereas the chemical nature of volatile materials is quite well understood. much less is known about non-volatile materials. One class of these compounds that contribute to the overall flavor impression of food are peptides. This paper discusses general and specific aspects of the sensory impacts that this defined class of compounds elicits. Emphasis will be given to correlations between the chemical structure of peptides and their taste contribution.

55.

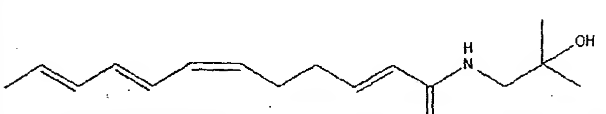
SAVORY PEPTIDES PRESENT IN MOROMI FILTRATE OBTAINED FROM SOY SAUCE FERMENTATION OF YELLOW SOYBEAN. ***Hanifah Nuryani Lioe**[1], Anton Apriyantono[2], Dedi Fardiaz[2], Budiatman Satiawihardja[2], Jennifer M. Ames[3], and Elizabeth L. Inns[3]. (1) Department of Food Technology and Human Nutrition, Bogor Agricultural University, Indonesia, Kampus IPB Darmaga, PO Box 220, Bogor, West Java 16002, Indonesia, Fax: 62-251-626725; 624546, hanilioe@hotmail.com, (2) Department of food technology and human nutrition, Bogor Agricultural University, (3) School of Food Biosciences, The University of Reading*

The presence of savory peptides in moromi filtrate has been investigated. Moromi filtrate was prepared by fermenting yellow soybean using Aspergillus oryzae as the starter at the first step (mold fermentation) and 20% brine solution at the next step (brine fermentation). The moromi was then ultrafiltered stepwise using membranes with MW cut-offs of 10,000, 3,000, and 500 Da, respectively.The fraction with MW < 500 Da was chromatographed using Sephadex G-25 SF to yield four fractions, 1-4. Analysis of soluble peptides, NaCl content, alpha-amino nitrogen, amino acid composition, peptide profile using CE coupled with DAD, taste profile and free glutamic acid content, were performed for each fraction. Fraction 2 contained a relatively high total glutamic acid content, but a relatively low free glutamic acid content and had the highest umami taste. This fraction also had more peptides containing non-aromatic amino acids than the other fractions. The peptides present in fraction 2 may play a role, at least in part, in its intense umami taste.

56.

PUNGENT AND TINGLING COMPOUNDS IN ASIAN CUISINE. ***Christophe C. Galopin**[1], Stefan M. Furrer[1], and Andreas Goeke[2]. (1) Ingredient Systems, Givaudan Flavors R&D, 1199 Edison Drive, Cincinnati, OH 45216, Fax: 513-948-3582, christophe.galopin@givaudan.com, (2) Fragrance Research, Givaudan Duebendorf Ltd*

Southern Asian cuisine is well known for its use of flavorful and pungent spices. The sanshool chemicals, such as alpha-hydroxy-sanshool from the Japanese Sancho pepper and other Asian peppers, are particularly interesting because they not only give a hot sensation in the mouth cavity but also a tingling effect on the tongue. In order to understand the effect of the sanshool chemicals we have synthesized a variety of derivatives. Tasting of those derivatives provided information about Structure Activity Relationship (SAR) for the tingling effect exhibited by these chemicals. Based on this study we are able to propose a minimal structure required for the tingling effect. We also used this SAR knowledge to design stable compounds with potential tingling effect.



alpha-hydroxy-sanshool

57.

SYNTHESIS, STRUCTURE, AND ACTIVITY OF NOVEL GLYCOCONJUGATES EXHIBITING UMAMI TASTE. ***Imre Blank**[1], Fabien Robert[1], Laurent B. Fay[1], Ersan Beksan[2], Thomas Hofmann[2], and Peter Schieberle[2]. (1) Nestle Research Center, Nestec Ltd, Vers-chez-les-Blanc, P.O. Box 44, 1000 Lausanne 26, Switzerland, Fax: +41 21 785-8554, imre.blank@rdls.nestle.com, (2) Deutsche Forschungsanstalt für Lebensmittelchemie*

Since recently, the so-called umami taste is accepted as the fifth basic taste quality along with the taste modalities sweet, sour, salty, and bitter. This is mainly due to the identification of the taste receptor for glutamate. Other compounds with similar sensory characteristics belong to the group of purine-5′-nucleotides. These compounds occur in many savory foods such as meat, fish, seafood, and mushrooms. They are also widely used as taste-enhancers in culinary products and snacks.

In this paper, we focus on structure elucidation, synthesis, and sensory properties of novel glycoconjugates, e.g. N-glucosyl glutamate and the Amadori compound fructosyl glutamate, which represent a new class of umami-tasting compounds. Their stability was studied by NMR measurements showing that the Amadori compound is much more stable as compared to the N-glucosyl derivative.

58.

TASTE-ACTIVE GLYCOCONJUGATES OF GLUTAMATE: NEW UMAMI COMPOUNDS. ***Hedwig Schlichtherle-Cerny**, Christoph Cerny, and Fabien Robert, Nestlé Research Center, Nestec Ltd, Vers-chez-les-Blanc, P.O. Box 44, CH-1000 Lausanne 26, Switzerland, Fax: +41-21-785-8949, hedwig.schlichtherle-cerny@rdls.nestle.com*

Hydrolyzed plant proteins are widely used as ingredients in culinary poducts for their glutamate-like "umami" taste. The comparison of the taste profiles of three different wheat gluten hydrolyzates revealed the enzymatic hydrolyzate of acid-deamidated wheat gluten to elicit an intense glutamate-like taste. The hydrolyzate was analyzed by "LC-tasting", a technique comprising stepwise fractionation of a food by different chromatographic methods, such as gel permeation chromatography and RP-HPLC, and the sensory evaluation of the obtained fractions after lyophilization. The chemical analysis of the most intense glutamate-like subfraction by hydrophilic interaction liquid chromatography coupled to electrospray ionization mass spectrometry (HILIC-ESI-MS) revealed many hydrophilic glutamyl di- and tripeptides, as well as the presence of different glycoconjugates of glutamate, glutamine, and lysine. The most abundant Amadori compound, *N*-(1-deoxy-fructos-1-yl) glutamate, was identified as eliciting an intense umami taste. Glycoconjugates of glutamate represent a new class of compounds which putatively impart umami taste to various foods.

59.

STABILITY OF CYCLIC α-KETO ENAMINES WITH COOLING EFFECT. ***Christoph Cerny**, Fabien Robert, and Renaud Villard, Nestlé Research Center, Nestec Ltd, Vers-chez-les-Blanc, P.O.Box 44, Lausanne CH-1000, Switzerland, Fax: +41-21-785-8554, christoph.cerny@rdls.nestle.com*

Recently a novel class of compounds eliciting a cooling sensation in the oral cavity and on the skin, with a cyclic α-keto enamine structure was discovered. We studied the stability of three of these new "cooling" compounds with low cooling thresholds, 5-methyl-2-(1-pyrridinyl)-2-cyclopenten-1-one (5-MPC), 5-methyl-4-(1-pyrridinyl)-3(2*H*)-furanone (5-MPF) and 4-methyl-3-(1-pyrridinyl)-2(5*H*)-furanone (4-MPF). The compounds were dissolved in deuterated chloroform and deuterated methanol/water, respectively, and stored at 20°C and 37°C for up to 3 months. The stability was followed by ^{1}H-NMR and GC/MS analyses. The 5-MPC showed only poor stability and isomerisation into 3-methyl-2-(1-pyrridinyl)-2-cyclopenten-1-one (3-MPC) occured. On the other hand, 5-MPF and 4-MPF were reasonably stable under both lipophilic and hydrophilic conditions and more than 75% survived at 37°C. The ^{1}H-NMR and GC/MS data suggest that in all three compounds the protons at the cyclopentene...

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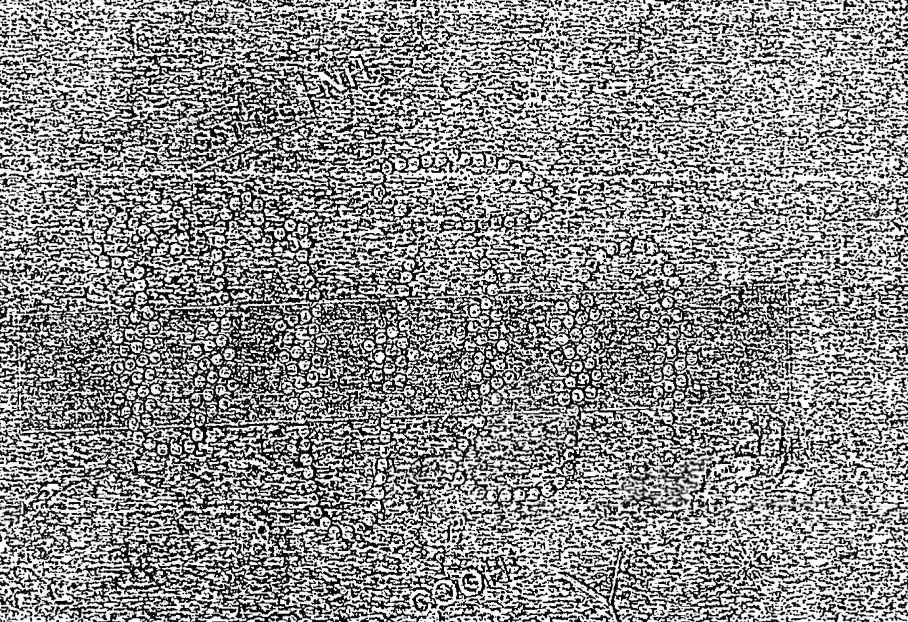
Challenges in Taste Chemistry and Biology



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Chapter 9

Pungent and Tingling Compounds in Asian Cuisine

Christophe C. Galopin[1], Stefan M. Furrer[1], and Andreas Goeke[2]

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Southern Asian cuisine is well known for its use of flavorful and pungent spices. The sanshool chemicals, such as alpha-hydroxy-sanshool from the Japanese Sanchoo pepper and other Asian peppers, are particularly interesting because they not only give a hot sensation in the mouth cavity but also a tingling effect on the tongue. In order to understand the effect of the sanshool chemicals we have synthesized a variety of derivatives. Tasting of those derivatives provided information about Structure Activity Relationship (SAR) for the tingling effect exhibited by these chemicals. Based on this study we are able to propose a minimal structure required for the tingling effect. We also used this SAR knowledge to design stable compounds with potential tingling effect.

Introduction

The research on pungent compounds has been very active in the past few years thanks to commercial and scientific interests. On the commercial side, consumer trends show an increased demand for strongly pungent flavors all over the world. This demand is created by Americans and Europeans who are more and more interested in spicy Asian and Latin American foods and by the

expanding Asian and Latin American markets. The classic pungent compounds, piperine and capsaicin, do not satisfy the consumers' need for "burn-to-death" pungency. On the scientific side, pungency is a very interesting area. Pungency is a mouthfeel which involves non-volatile molecules that interact with trigeminal nerves. In contrast with cooling, which involves cold thermoreceptor, pungency (or hotness) involves trigeminal pain nerves. In fact, many pungent chemicals are weak anesthetics as they saturate the pain nerve response preventing any further pain signal from being transmitted to the brain. Pungency can therefore be described as a pleasurable pain in the mouth.

Thanks to our TasteTrek™ expeditions to Asia and to our interest in Sanshoo pepper, we became interested not only in pungent chemicals but also in chemicals that create a tingling sensation on the tongue. It has been reported that long-chained amides from the sanshool and bungeanool families exhibit pungent and tingling properties and have long been used as anesthetics in folk medicine (*1*). Nevertheless, these chemicals are difficult to synthesize and are often unstable (*2*). We wondered whether we could stabilize these molecules by removing unnecessary features. Although it was noticed that one of the cis-double bond in the fatty chain was a key element of activity (*3*), little structure activity relationship (SAR) information is available. Here we wish to describe our research to identify the elements of sanshools and bungeanools that are required for pungency. We will show how that knowledge can be applied to the synthesis of new molecules with the desired properties.

Experimental

Methyl (2E,4E,8Z,11Z)-tetradeca-2,4,8,11-tetraenoate 21

To a solution of methyl 4-(diethoxyphosphoryl)crotonate (4.66g (19.7 mmol) in THF (50 ml) was added ^{t}BuOK (2.40g, 19.7 mmol) at 0°C and the mixture was stirred for 30 minutes. The red-brown solution was cooled to –30°C and (4Z,7Z)-decadienal 20[1] (1.90g, 13.2 mmol) was added dropwise. The mixture was warmed to room temperature during 30 minutes and poured into a saturated solution of NH_4Cl. The mixture was extracted with MTBE, the organic phase was washed with water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The yellow residue was purified by chromatography to yield 1.31g (45%) of a yellowish oil (containing about 10 % of the 4Z-isomer). ^{1}H-NMR (400MHz, $CDCl_3$) (δ in ppm): 7.26 (dd, J = 15.6, 10.0 Hz, 1H), 6.21-6.08 (m, 2H), 5.80 (d, J = 15.6 Hz, 1H), 5.44-5.25 (m, 4H), 3.74 (s, 3H), 2.77 (dd, J = 7, 7 Hz, 2H), 2.25-2.15 (m, 4H), 2.07 (dq, J = 7, 7 Hz, 2H), 0.97 (t, J = 7 Hz, 3H); ^{13}C-NMR (100MHz, $CDCl_3$): 167.6 (s), 145.1 (d), 143.8 (d), 132.0 (d), 129.1 (d), 128.7 (d), 128.4 (d), 126.9 (d), 119.0 (d), 51.4 (q), 32.9 (t), 26.4 (t), 25.5 (t), 20.5 (t), 14.2 (q); MS (EI): 234 (M^+, 1), 129 (2), 203 (3), 175 (14), 152 (17), 133 (10), 119 (12), 105 (14), 93 (15), 67 (100), 59 (9), 55 (26), 41 (15); IR (neat): 3011w, 2962m, 1719s, 1644m, 1435m, 1251s, 1135s, 999s, 723m cm^{-1}.

Bungeanool 7

Ester **21** (2.00g, 8.5 mmol) was dissolved in water/MeOH (30 ml, 1:3) and saponified with KOH (1.67g, 30 mmol) overnight. The mixture was brought to acidic pH with ice-cold HCl and extracted with MTBE. The organic phase was washed with water and brine, dried ($MgSO_4$) and concentrated *in vacuo* to yield 1.52g of the (2*E*,4*E*,8*Z*,11*Z*)-tetradeca-2,4,8,11-tetraenoic acid. This was dissolved in CH_2Cl_2 (30 ml) containing a drop of DMF. Oxalyl chloride (5.08g, 40 mmol) was added dropwise and the mixture was stirred for 8h at room temperature. The solvent and the excess of oxalylchloride were evaporated and the residue was dried *in vacuo*. The oily material was again taken up in CH_2Cl_2 and 1-amino-2-methyl-2-propanol (1.25g, 14 mmol) was added. The mixture was stirred for 1h, the solvent was evaporated and the residue purified by chromatography to yield 0.98g (40%) of bungeanool **7** as a slightly yellow oil. ^{1}H-NMR (200MHz, $CDCl_3$) (δ in ppm): 7.21 (dd, J = 15 , 11 Hz, 1H), 6.33 (bt, J = 6Hz, 1H), 6.20-6.05 (m, 2H), 6.85 (d, J = 15 Hz, 1H), 5.47-5.25 (m, 4H), 3.35 (d, J = 6 Hz, 2H), 2.77 (dd, J = 7, 7 Hz, 2H), 2.25-2.16 (m, 4H), 2.07 (dq, J = 7, 7 Hz, 2H), 1.23 (s, 6H), 0.97 (t, J = 7 Hz, 3H).

N-isobutyl (2E,4E,8Z)-undeca-2,4,8-trienamide 28

At 0°C, in a round-bottom flask under an inert atmosphere of nitrogen, a solution of 2.77g (11mmol) of diethyl diethyl N-isopropyl phosphonoacetamide in 20mL of dry tetrahydrofuran is added to 15.5mL of a 1.5M solution of butyl lithium (23mmol) in hexane. The mixture is stirred at 0°C for thirty minutes. A solution of 1.4g of E2;Z6-nonadienal in 5mL of dry tetrahydrofuran is then added dropwise to the stirred reaction mixture. The mixture is stirred at 0°C for two hours. The reaction mixture is then diluted in 100mL of hexane and washed with a saturated aqueous solution of ammonium chloride. The organic phase is collected and dried over anhydrous magnesium sulfate, filtered and concentrated. The residue is purified by chromatography on silica gel with EtOAc/Hexane:2/8 as the eluent to give 0.5g of product as a white fluffy powder. ^{1}H NMR (300MHz in $CDCl_3$) (δ in ppm): 7.2 (dd, J=15, 10.2 Hz, 1H), 6.1 (m, 2H), 5.75 (d, J=15 Hz, 1H), 5.34 (m, 3H), 3.2 (t, J=6.5Hz ,2H), 2.2 (m,

2H), 2.0 (quintuplet, J=7.5Hz, 1H), 1.8 (septuplet, J=6.6Hz, 1H), 0.96(t, J=7.5Hz, 3H), 0.93 (d, J=6.9Hz, 3H).

Methyl (2E,4E,8Z)-deca-2,4,8-trienoate 30:

To a solution of methyl 4-(diethoxyphosphoryl)crotonate (11.6 g, 49.2 mmol) in THF (70 ml) was added ^{t}BuOK (5.98g, 49.2 mmol) at 0°C. The mixture was cooled to −78°C and a solution of (*Z*)-hex-4-enal (4.00g, 40.8 mmol) in THF (10 ml) was added dropwise. After the cooling bath was removed and the mixture had warmed up to room temperature, sat. NH_4Cl was added and the mixture was extracted with pentane. The organic phase was washed with water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was distilled bulb to bulb (90°C/0.01 Torr) to yield 30 (2.4g, 33%) as a 7/3 mixture of the (4*E*/*Z*)-isomers. ^{1}H-NMR (200MHz, $CDCl_3$) (δ in ppm): 7.69-7.20 (m, 1H), 6.29-5.31 (m, 5H), 3.76, 3.74 (2s, 3H), 2.45-2.13 (m, 4H), 1.61 (d, J = 6.5 Hz, 3H); MS (EI): 180 (M^+, 2), 149 (6), 121 (10), 111 (27), 93 (28), 67 (51), 59 (32), 55 (100), 39 (35), 29 (28); IR (neat): 3015m, 2949m, 1720s, 1644m, 1435m, 1264s, 1137m cm^{-1}.

N-(2-hydroxy-2-methyl-propyl) (2E,4E,8Z)-deca-2,4,8-trienamide 29

Ester 30 (1.90g, 10.56 mmol) was saponified with NaOH (2.11g, 52.8 mmol) in H_2O/MeOH (5/1, 60 ml) for 2 days. The crude reaction mixture was brought to pH = 1 with HCl (2N) and extracted 5 times with MTBE. The organic phase was washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was dissolved in CH_2Cl_2 (30 ml) containing a drop of DMF and treated overnight with oxalyl chloride (2.0g, 15.7 mmol). The solvent was removed in vacuo (while keeping the temperature around 20°C), the residue was redissolved in CH_2Cl_2 (10 ml) and added to a solution of 1-amino-2-methyl-2-propanol (1.1g, 12.4 mmol) and triethyl amine (1.5g, 15 mmol) in CH_2Cl_2 (20 ml). The mixture was stirred for 5h and was then quenched with water and extracted with CH_2Cl_2. The organic phase was washed with 1N HCl, water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. *N*-(2-hydroxy-2-methyl-propyl) (2*E*,8*Z*)-deca-2,4,8-trienamide 29 (2.0g, 80%) crystallized from ethyl acetate/hexane as a 7/3 mixture of the (4*E*/*Z*)-isomers in form of slightly yellow crystals. (4*E*)-Isomer: ^{1}H-NMR (400MHz, $CDCl_3$) (δ in ppm): 7.19 (dd, J = 15.0 Hz, 10.3 Hz, 1H), 6.56 (broad t, J = 6.0 Hz, 1H), 6.19-6.03 (m, 2H), 5.86 (d, J = 15.0 Hz, 1H), 5.52-5.44 (m, 1H), 5.39-5.32 (m, 1H), 3.49 (s, 1H), 3.33 (d, J = 6.0 Hz, 2H), 2.25-2.13 (m, 4H), 1.60 (d, J = 6.5 Hz, 3H); MS (EI): 237 (M^+, 4), 179 (62), 164 (13), 149 (23), 124 (48), 110 (100), 94 (22), 84 (25), 66 (30), 59 (47), 55 (88), 41 (24), 30 (34); IR (neat): 3287br(OH), 2974m, 2931m, 1658s, 1627s, 1609s, 1537s, 1179m, 1161m, 996m, 913m cm^{-1}.

Example of the synthesis of a cinnamamide.

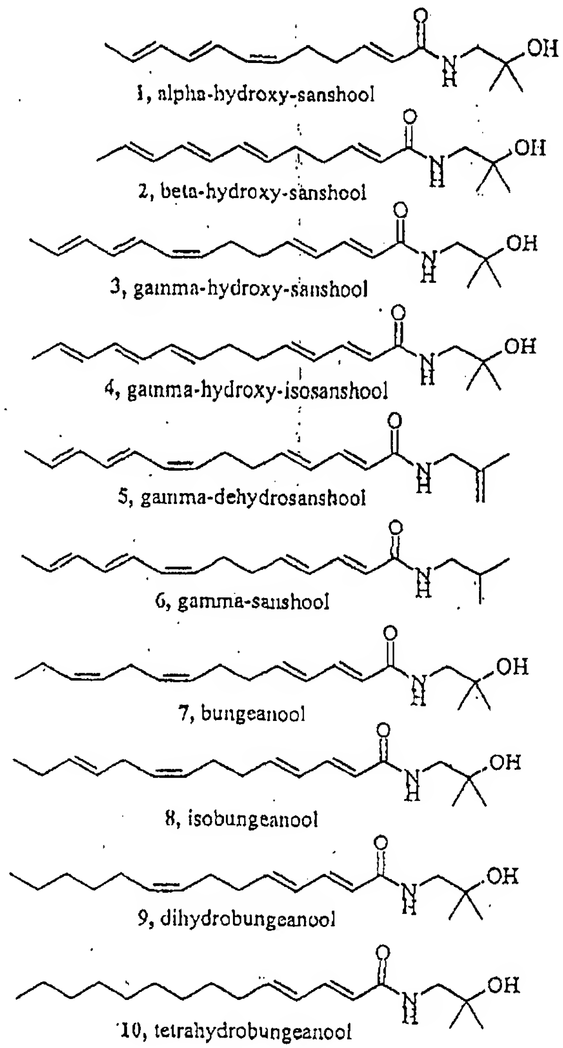
In a round-bottom flask under an inert atmosphere of nitrogen, cinnamic acid (37.04g, 0.25 mol) and thionyl chloride (44.6g, 0.375mol) were dissolved in tetrahydrofurane. Two drops of pyridine were added and the mixture was heated at reflux for 4h. The red mixture was concentrated (40°C / 125mbar) and 42.7 g of crude cinnamyl choride were recovered as a brownish oil. In a round-bottom flask under an inert atmosphere of nitrogen, cinnamyl chloride (4.1 g, 25 mmol) is dissolved in a mixture of 25ml of dry tetrahydrofuran contain and 5 ml of pyridine was added. To this solution, propylamine (1.77g, 30mmol) was added over a period of 30 minutes at room temperature. The mixture was stirred for 5h at room temperature. The reaction mixture was diluted with MTBE and extracted with water. The organic phase was washed with aqueous hydrochloric acid (1N) and brine, dried ($MgSO_4$), filtered and concentrated. The residue was crystallized from MTBE/hexane to give 4.1g of product as a yellowish fluffy powder. ^{1}H NMR (300MHz, $CDCl_3$) (δ in ppm): 7.6 (d, J= 15.6Hz 1H), 7.5 (m, 2H), 7.4 (m, 3H), 6.4 (d, J= 15.9Hz, 1H), 5.8 (broad s, 1H), 3.4 (q, J= 6.7Hz, 2H), 1.6 (sextuplet, J= 7.3Hz, 2H), 1.0 (t, J= 7.3Hz, 3H).

Sanshool and Bungeanool Families

General description

Sanshools and bungeanools (Figure 1) are both long-chained polyenamides found in the *Achillea*, *Echinacea* and *Zanthoxylum* plant species. It seems that α-sanshool, a.k.a. echinacein and neoherculin, was first isolated from *Echinacea angustifolia* (4) and *Zanthoxylum piperitum* (Sanshoo pepper) (5) and later from *Zanthoxylum clava-herculin* (6). Bungeanools were first recognized as a family when isolated from *Zanthoxylum bungeanum*[2] (7) although similar chemicals had been described earlier (8).

The main difference between sanshools (1–6) and bungeanools (7–10) is the presence of three conjugated double bonds at the end of the amide chain of sanshools whereas bungeanools only have two or less unconjugated double bonds. Moreover, sanshools are either α,β or α,β,γ,δ unsaturated amides



1, alpha-hydroxy-sanshool
2, beta-hydroxy-sanshool
3, gamma-hydroxy-sanshool
4, gamma-hydroxy-isosanshool
5, gamma-dehydrosanshool
6, gamma-sanshool
7, bungeanool
8, isobungeanool
9, dihydrobungeanool
10, tetrahydrobungeanool

Figure 1 Examples of sanshools and bungeanools

whereas all bungeanools seem to be α,β,γ,δ unsaturated amides. In both families, the N-alkyl group is predominantly 2-hydroxy-2-methylpropane, but chemicals with dehydrated (5) or dehydroxylated (6) groups have been reported *7, 9*). Interestingly enough, the first sanshool isolated had no hydroxyl group on the N-alkyl chain so the word "sanshool" refers to a non-functionalized N-alkyl group whereas "bungeanool" refers to a hydroxylated N-alkyl group.

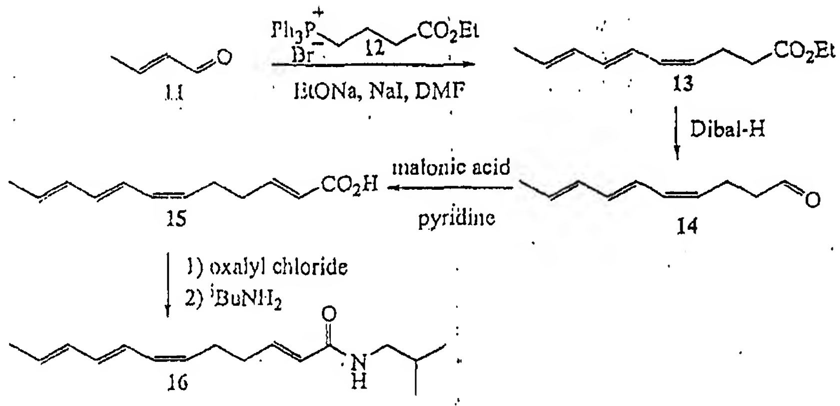
Chemical Synthesis

The difficulty of the synthesis of these chemicals depends on the ease of synthesis of the intermediate aldehydes such as **14** and **20**. These aldehydes are often expensive and complex to synthesize (*10*). Scheme 1 and 2 show examples of synthesis of α-sanshool (*2*) and bungeanool. Almost all chemicals in either family can be obtained by using similar techniques.

SAR Study of the Fatty Chain

In order to establish an SAR for these chemicals, we decided to synthesize a small series of sanshools, bungeanools and derivatives, and screen them for pungency. We decided to synthesize derivatives with a variety of functionalities representative of, both families. These derivatives are α,β and α,β,γ,δ unsaturated amides with up to three unsaturations at the end of the chain. We also made some arachidonic acid derivatives (23–25) that have no conjugated double bonds.

From the pungency results shown in Figure 3, it can be concluded that having a *cis*-double in the chain is indeed a key element (*3*) but it is not the only one. The inactivity of the arachidonic derivatives show that a certain motif must be preserved. The activity of compound **22** indicates that the long chain does play a role in pungency. The activity of compound **10** indicates that the end of the chain must be unsaturated but the activity of compound **4** suggests that the unsaturation must follow a certain pattern. It becomes apparent that all active compound share a common motif (CH=Z=CH-CH2-CH2-CH=E=CH) in addition to the amide function. This motif cannot be branched (**27**) and although it seems required it is not enough to give activity (**25**). Finally, the hydroxy group on the N-alkyl group does not seem to be required since **16** and **1** are both pungent.

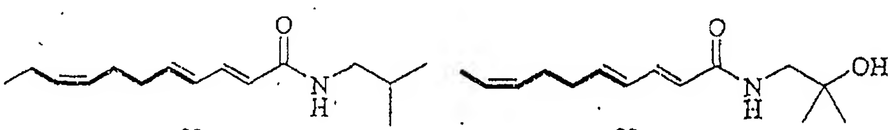


Scheme 1: Synthesis of α-sanshool

As a result of our observations we propose the model in Figure 4 as a good representation of the features require for sanshool and bungeanool-type chemicals to be pungent.

Figure 4 shows that the N-isobutylcarboxamide and the (CH=Z=CH-CH2-CH2-CH=E=CH) motif are required for pungency. However, some optional features enhance the pungent character of the molecule (hydroxyl group on N-alkyl group, unsaturation, longer chain). We noted that pungency was only noticeable when molecules had the required features plus two optional features.

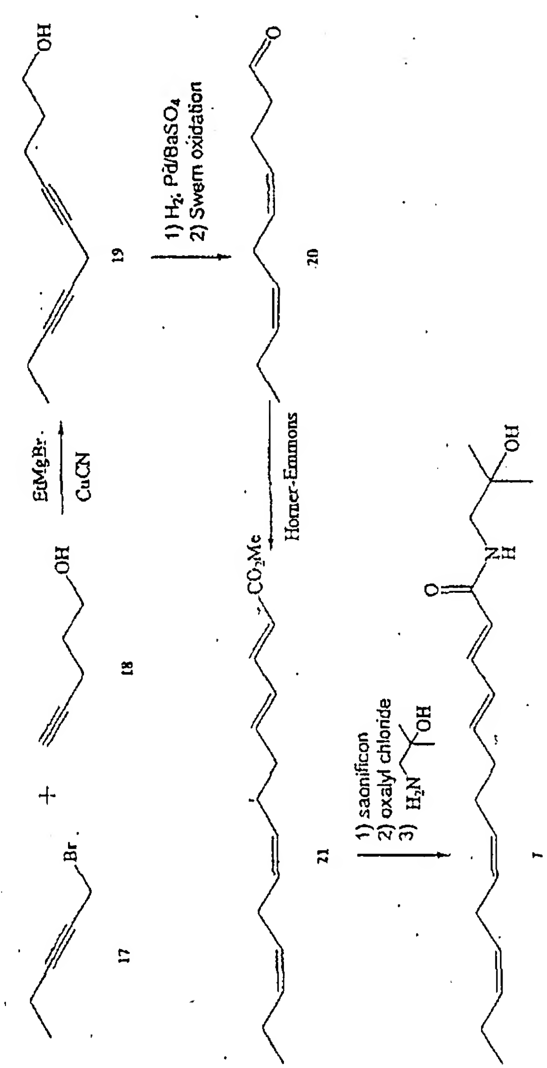
To test our model we designed two new molecules 28 and 29 that follow the rules shown in Figure 4.



28 29

These molecules were very interesting because we expected that the absence of a triene system would stabilize the molecule, these structures had never been reported before, and their fatty chain could easily be made from commercially-available aldehydes 29 and 31 (Scheme 3). Amide 28 was of particular interest since we could synthesize it in one step by modification of a published method (Scheme 3) (11).

This experiment allowed us to validate our model since 28 and 29 exhibited a pungency typical of that of the sanshool and bungeanool families. Neat amides 28 and 29 showed enhanced stability properties probably because they could be obtained as white powders instead of thick oils. The crystalline matrix may slow down the polymerization reaction. While 29 was more pungent, 28 was easier to synthesize thanks to a one-pot reaction.



Scheme 2: Synthesis of bungeanool

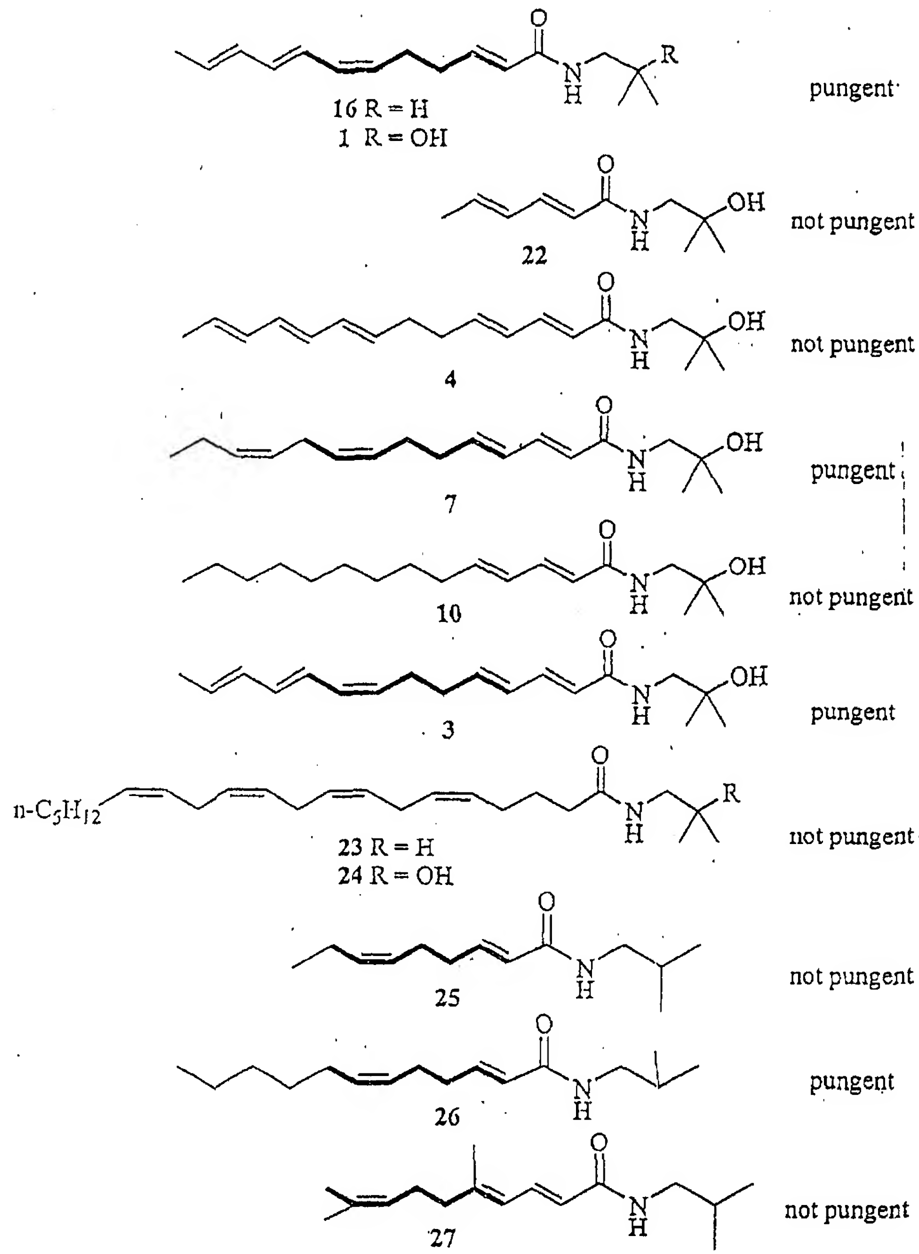
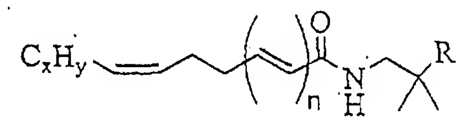


Figure 3 Activity of some sanshool and bungeanool derivatives

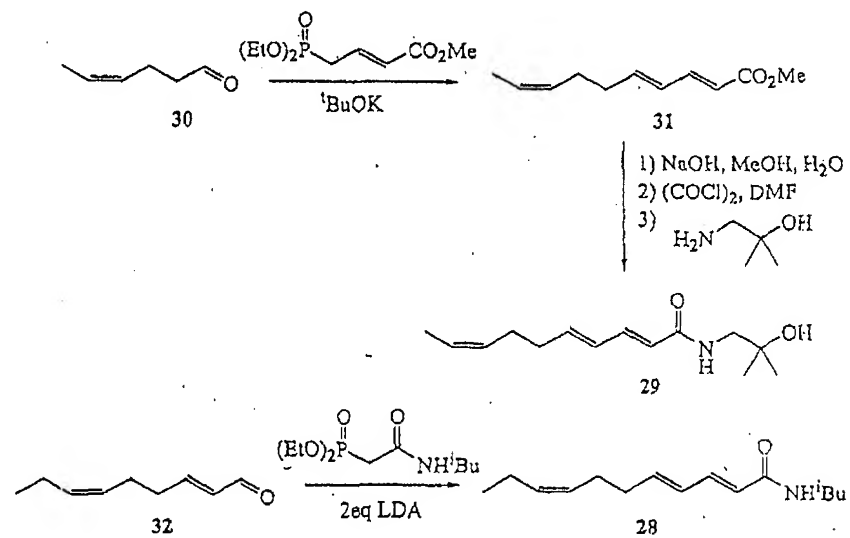


Minimal Structure: R=H, n=1, x=1

Optional Features: R=OH, n=2, x > 2

Noticeable Pungency = Minimal Structure + two Optional Features

Figure 4 Proposed structural requirements



Scheme 3 Synthesis of 28 and 29

Application of the SAR Study of the Fatty Chain

It appeared to us that the only way to stabilize these molecules was to eliminate all unsaturation at the end of the chain. This was however impossible since we showed that at least one *cis*-double bond is needed at the end of the chain. We came up with the idea that the *cis*-double bond may be replaced by a phenyl group. In fact we realized that there may be three different ways that the chain could wrap up so that it would sterically look like a phenyl group (Figure 5).

To test this idea a series of phenyl-containing amides was prepared, a few examples are shown in Figure 6.

All the chemicals made in this series were stable at ambient temperature but only 35 showed a noticeable pungency. As far as we know, this simple cinnamamide had never been described as being pungent. Unfortunately, 35 is very weak and does not have the tingling character of the sanshool and bungeanool families.

SAR Study of the N-Alkyl Group

Although 35 was not a viable solution to our stability problem, it gave us a very accessible skeleton that we could use to vary the N-alkyl group. A series of cinnamamides was synthesized with the N-alkyl groups shown in Figure 7.

None of the new cinnamamides was pungent, which indicated that the isobutyl group was indeed required for pungency.

Conclusion

We have shown that a model could be built to predict whether a polyenamide of the sanshool or bungeanool type was pungent or not. We were able to validate the model by synthesizing unknown structures that fit the model and were found to be pungent. We were able to adapt the model to create a phenyl containing amide that had a pungent character. The activity of cinnamamide 35 suggests that sanshools and bungeanools must be activate their corresponding heat and tactile receptors as conformers were the fatty chain is wrapped up to activate. This theory will be difficult to prove until we have more information about the receptor, with which these chemicals are binding.

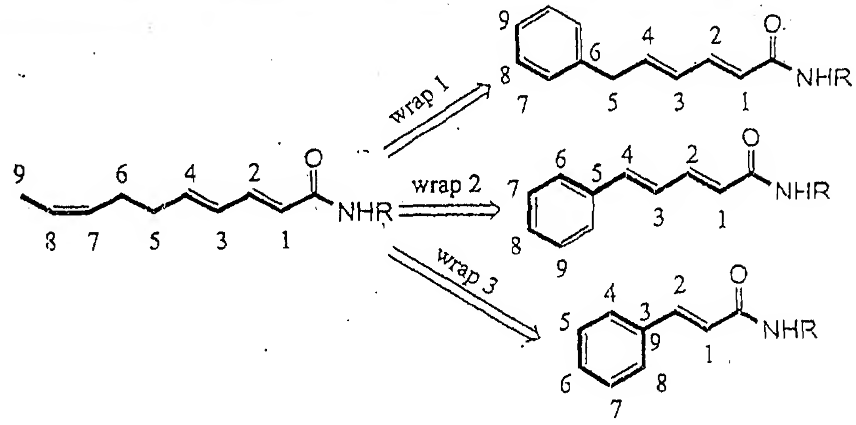


Figure 5 Wrapping of the fatty chain of a minimal pungent structure

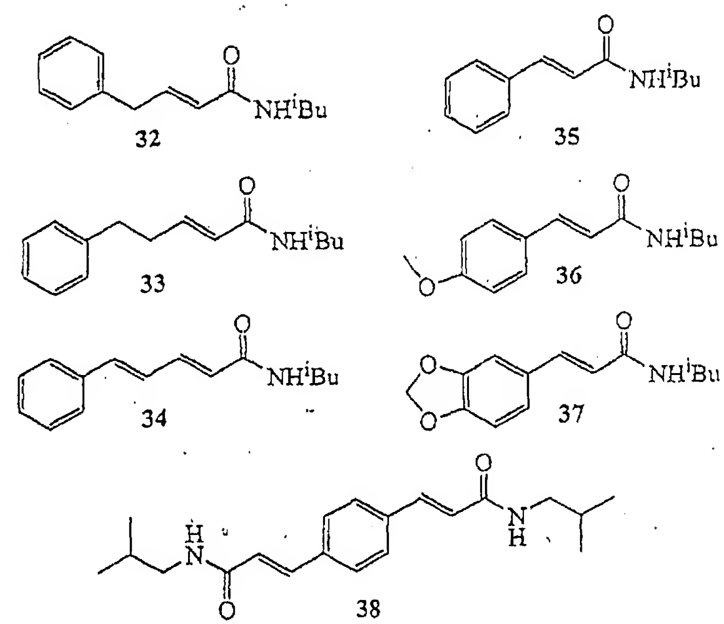


Figure 6 Some phenyl containing amides that fit the "wrapped" model

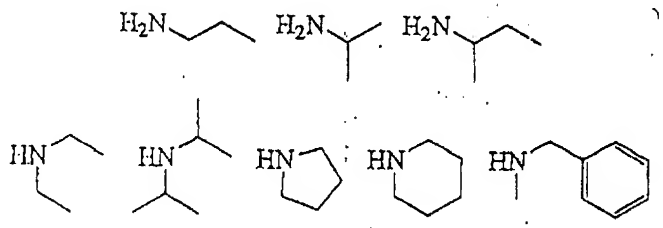


Figure 7 Various amines used to make cinnamamides

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Chapter 10

Structural Requirements for the Cooling Activity of Cyclic α-Keto Enamines

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[2]Deutsche Forschungsanstalt für Lebensmittelchemie, Lichtenberstrasse 4, D–85748 Garching, Germany

3-Methyl- and 5-methyl-2-(1-pyrrolidinyl)-2-cyclopenten-1-one were recently identified as cooling compounds formed by Maillard reaction in heated glucose/L-proline mixtures, as well as in roasted malt. To gain more insights into the molecular requirements of this cooling effect, a range of cyclic keto enamine derivatives were synthesized, and their physiological cooling activities were evaluated. Any modification of the amino moiety, the carbocyclic ring size, or the alkyl substitution led to an increase of the cooling threshold. Insertion of an oxygen atom into the carbocycle, however, increased the cooling activity, e.g. the threshold of the corresponding3(2*H*)-furanone was 16-fold below the threshold concentration found for the 2-cyclopenten-1-one. Incorporation of an oxygen into the 5-position of the cyclopentenone resulted in a even more drastic effect, e.g. the 2(5*H*)-furanone exhibited the strongest cooling effect at the low threshold of 0.02-0.06 mmol/L. In contrast to the minty smelling (–)-menthol, these keto enamines are odorless, but impart a cooling sensation to the oral cavity and to the skin.

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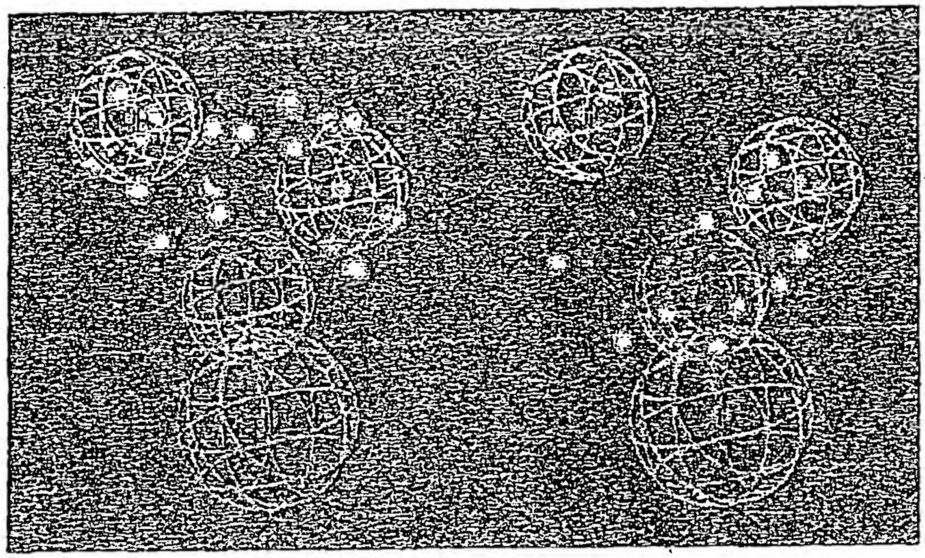

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Prefac

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The world of non-volatiles: heating compounds for today and tomorrow

Christophe C. Galopin

Givaudan Flavours Corp., Research and Development Dept., Ingredient Systems Group, 1199 Edison Drive, Cincinnati OH 45216, USA.

Abstract

Four new commercially interesting pungent compounds are presented along with a short review of piperine and capsaicin. Advantages, drawbacks and differences are discussed. An insight on synthesis and commercial availability is also given.

Introduction

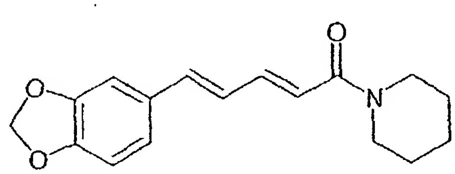
Flavour companies have contemplated the world of non-volatiles for many years. These compounds have a special effect in the mouth with no or little aroma and often elude chemists who rely solely on GC data for analysis. Non-volatiles are believed to be essential for the reconstitution of many fruit and vegetable flavours where the aroma alone fails to describe the real taste of the botanical. Those non-volatiles are often very difficult to isolate because they cannot be identified by simple GC-O techniques. Moreover, few people know how to describe mouthfeel and how to separate it into its basic components.

However, non-volatile research has been active for a long time in the area of pungency; certainly because it is the mouthfeel effect that is the easiest to describe. Since the nineteenth century, piperine and capsaicin have been known as the pungent principle of black and red pepper, respectively. These two compounds have been widely used in flavour industry when a pungent sensation is desired without pepper flavour or to boost the pungency of pepper flavours. Although these compounds are still of use today they may fall short of customers' expectations for stronger burning sensations.

In the past decade, Givaudan has put a lot of effort into the identification and commercialisation of new pungent compounds. After a short review of piperine and capsaicin, we wish to report findings on three new pungent compounds isolated during our Tastetrek expeditions in Gabon and China, as well as one artificial derivative.

Pungent ingredients of today

Piperine



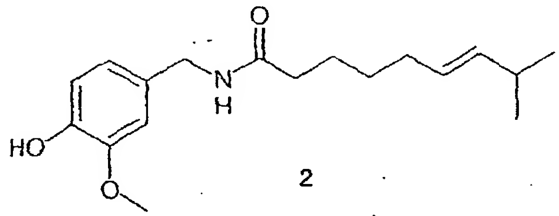
1

Piperine **1** was first isolated from black pepper in 1821 (Pelletier, 1821; Pelletier, 1832). It has been described as virtually odourless and creating a hot, burning sensation in the back of the mouth and near the throat (Arctander, 1969). It is widely used in flavours when mild pungency is required.

Many syntheses of piperine have been described and the most practical one seems to be the simple amidation of chavicinoyl chloride with piperidine (Arctander, 1969; Lohaus,

1928). Nevertheless, a simple aldolisation reaction of heliotropine should not be ignored (Schultze and Oediger, 1981). Black pepper oleoresin can also be used as a natural substitute for piperine.

Capsaicin



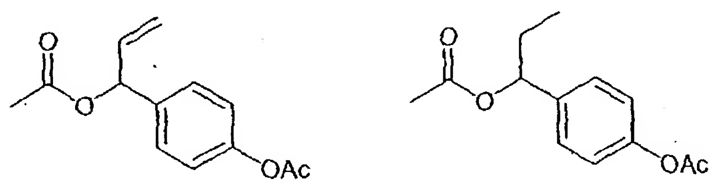
2

Capsaicin 2 was first isolated from *Capsicum* in 1876 (Thresh, 1876). It has been described as having a mild warm-herbaceous odour and a burning-pungent taste. It is widely used in flavours to enhance the pungency of flavour composition. It is considered characteristic of red pepper pungency.

Capsaicin can be made from iso-decenyl chloride and vanillylamine, however synthesis of the iso-decenyl part can be challenging (Kaga *et al.*, 1996). As a result, a related compound, called synthetic capsaicin, made from nonanyl chloride and vanillylamine is often preferred. A natural substitute of capsaicin are *Capsicum* oleoresins.

Pungent ingredients for tomorrow

1'-acetoxychavicol acetate and derivatives



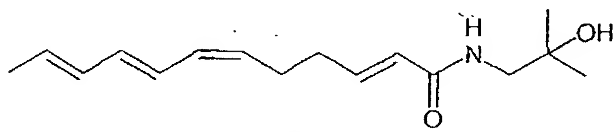
3 4

Givaudan recently reported the identification of 3 as the pungent component of *Alpinia galangal* (Yang and Eilerman, 1999). Although it has been described as less pungent than capsaicin, it is much easier to synthesise (Gautschi *et al.*, 1999), a feature that makes it an interesting substitute of capsaicin.

One major drawback of 1'-acetoxychavicol acetate (ACA) is its instability in water. We determined (Yang and Eilerman, 1999) that the instability of 3 was due to a sigmatropic rearrangement that produced a non-pungent component. The rearrangement of ACA 3 was noticed to be faster in aqueous solutions, a known feature of this type of rearrangement (Ganem, 1996).

As a result of a structure activity relationship study (Gautschi *et al.*, 1999), compound 4 was shown to be stable and as pungent as ACA 3. Although 4 is an artificial ingredient, it can be widely used where a strong pungency is required and price-constraint forbid the use of capsaicin.

Sanshool



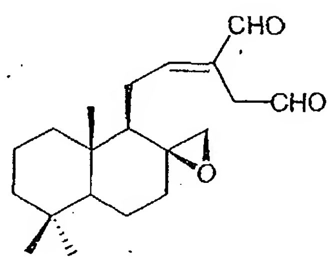
5

Long-chained unsaturated alkylamides such as alpha-hydroxysanshool 5, have been isolated from *Sansho*, *Huajiao* and *Zanthoxylum* species (Xiong *et al.*, 1997; Ito *et al.*, 1997). Alpha-hydroxysanshool and gamma-hydroxysanshool were identified as pungent by a Monell research group (Bryant and Mezine, 1999). These findings were confirmed by a study run at the same time at Givaudan on the pungent principle of Sansho peppers. Our Givaudan Tastetrek in China in 2001 has also identified alpha-hydroxysanshool as the pungent principle of several Chinese dishes.

Nevertheless, the pungency of sanshool chemicals is not their most interesting characteristic. Sanshool compounds also give a unique tingling sensation in the mouth accompanied by a mouth-watering effect. These compounds can be used in mildly pungent preparations where a special mouthfeel is sought.

Syntheses of sanshool chemicals involve at least five steps and may require the use of non-readily available materials (Sonnet, 1969; van der Linde *et al.*, 1985; Crombie and Fisher, 1985). They are also unstable and tend to decompose even when stored under nitrogen in the cold. These physical characteristics unfortunately make them difficult to use as single ingredients.

Aframodial



6

Aframodial 6 was recently identified as the pungent principle of the seeds of wild ginger plants harvested during our Tastetrek in Gabon in 1999. Chemically, this compound is very different from the others since it does not have any amide bond. Nevertheless it belongs to a known family of pungent dialdehydes like isovelleral or cinnamodial (Szállasi *et al.*, 1998).

The synthesis of this compound is simple but long and not chemically efficient (Kim and Isoe, 1983). Nevertheless, it is interesting to notice that, like ACA 3, this compound was also found in galangal (Hiroshi and Hideji, 1988). Aframodial may be useful as a pungency booster of ACA.

Conclusion

Although many new pungent compounds can be found in nature, few are as versatile as capsaicin or piperine. Nevertheless, the discovery of these new pungent compounds gives us access to new structures with pungent activity. The interest may not be in these new compounds themselves but in the derivatives than can be made from them.

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